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EXAMINER
COLLINS, CYNTHIA E

ART UNIT	PAPER NUMBER
1638	23

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/530,209	Applicant(s) INZE ET AL.	
	Examiner Cynthia Collins	Art Unit 1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,6-8,10,27 and 30-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-8, 10, 27, 30-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Amendment filed August 29, 2002, paper no.20, has been entered.

Claims 5, 9, 11-26, 28 and 29 are cancelled.

Claims 1, 2, 4, 6, 7, 8, 10 and 27 are newly amended.

Claims 30-41 are newly added.

Claims 1-4, 6-8, 10, 27 and 30-41 are pending.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claims 1-4, 6-8, 10 and 27 remain rejected, and newly added claims 30-41 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed March 25, 2002.

Applicant's arguments filed August 29, 2002, have been fully considered but they are not persuasive.

Applicant points out that the application describes a mitogenic cyclin function for the protein encoded by SEQ ID NO:2, that the specification discloses the meaning of the term "mitogenic" as well as the term "cyclin", that Example 1 describes the identification of a cell cycle interacting protein LDV59, that Example 4 describes the mitogen inducible nature of

LDV59 as Example 4 teaches a northern blot analysis revealing that the LDV59 gene is specifically induced by the mitogenic agents cytokinin and sucrose, and that further support for the description of the protein encoded by SEQ ID NO:2 as a mitogenic cyclin is found on pages 5 to 7 of the specification (reply pages 6-7).

The Office maintains that defining the terms "mitogenic" and "cyclin" is not sufficient to support a description of a nucleic acid encoding a protein that has a cyclin function. With respect to Example 1, the Office notes that Example 1 describes the isolation of an isolated nucleic acid of SEQ ID NO:1 encoding a protein of SEQ ID NO:2 that interacts with CDC2aAt in an *in vitro* yeast two-hybrid assay and that has homology to *Arabidopsis* D-type cyclins. With respect to Example 4, the Office notes that Example 4 describes the induction by cytokinin and sucrose of an RNA transcript that hybridizes to an isolated nucleic acid of SEQ ID NO:1. With respect to pages 5 to 7 of the specification, the Office notes that pages 5-7 describe the nature of the homology between the amino acid sequence of SEQ ID NO:2 and the amino acid sequences of other *Arabidopsis* D-type cyclins. While these observations suggest a correlation between the structure of SEQ ID NOS: 1 and 2 and D-type cyclins, they do not demonstrate that SEQ ID NO:1 encodes a protein that activates a cyclin-dependent kinase.

In response to the Examiner's comment that the specification does not describe sequences encoding an amino acid sequence at least 70% identical to SEQ ID NO:2, Applicant points to page 5 which indicates that the novel mitogenic gene of the present invention is designated LDV59 or CYCD4;1, to page 6 that teaches that CYCD4;1 only shows significant sequence similarity to other *Arabidopsis* D-type cyclins within its amino terminal domain and especially

with respect to the cyclin box. Applicant argues that considering only the cyclin box region, the CYCD4;1 protein has an amino acid sequence identity of 61.3%, 69.8% and 66.6% with other known *Arabidopsis* D-type cyclins, such that the presently claimed DNA sequences encoding an amino acid sequence at least 70% identical to the amino acid sequence of SEQ ID NO:2 are described (reply page 7).

The Office maintains that Applicant has described and characterized only one amino acid sequence, the amino acid sequence of SEQ ID NO:4, as the prior art has described and/or characterized the amino acid sequences of other known *Arabidopsis* D-type cyclins. Applicant has not described or characterized any novel polypeptide at least at least 70% identical to the amino acid sequence of SEQ ID NO:2 other than the polypeptide of SEQ ID NO:2.

In response to the Examiner's comment that the specification does not describe sequences hybridizing to SEQ ID NO:1, Applicant points to page 7 as describing such sequences (reply page 8).

The Office maintains that while page 7 does describe hybridizing conditions that may be used to isolate sequences that hybridize to SEQ ID NO:1, page 7 does not describe the structure and function of any nucleic acid sequence isolated under said conditions that encodes a protein that activates a cyclin-dependent kinase.

Applicant argues that the written description requirement does not presently nor has it ever demanded exemplification or even a reduction to practice of the claimed invention, and points out that Applicant may use indicia other than reduction to practice to show possession.

Applicant argues that an amino acid sequence identity of greater than 70% to SEQ ID NO:2 or a DNA which hybridizes under stringent conditions to SEQ ID NO:1 provides such relevant identifying characteristics sufficient to show Applicant's possession of the claimed invention (reply page 8).

The Office maintains that while Applicant may use indicia other than reduction to practice to show possession, in the instant case Applicant has not described any polypeptide having an amino acid sequence identity of greater than 70% to SEQ ID NO:2 which one skilled in the art would recognize as a protein that activates a cyclin-dependent kinase, or any DNA which hybridizes under stringent conditions to SEQ ID NO:1 which one skilled in the art would recognize as encoding a protein that activates a cyclin-dependent kinase.

Claims 2, 3, 10 and 28 remain rejected, and newly added claims 38-41 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the office action mailed March 25, 2002.

Applicant's arguments filed August 29, 2002, have been fully considered but they are not persuasive.

Applicant repeats, reasserts, and incorporates by reference the arguments set forth with respect to written description. Applicant argues that the present application teaches the isolation of many different nucleotide sequences which either code for amino acid sequences having greater than 70% identity to SEQ ID NO:2 or which hybridize under stringent conditions to SEQ

ID NO:1. Applicant argues that the specification teaches a mitogenic function for the protein encoded by SEQ ID NO:1. Applicant points out that the law does not require a specific example of everything within the scope of broad claims and does not require any specific working examples (reply pages 9- 10).

The Office maintains that the present application teaches only one isolated nucleic acid sequence encoding a polypeptide of SEQ ID NO:2 having amino acid homology to known D-type cyclins, the nucleic acid sequence of SEQ ID NO:1, and that the specification asserts but does not provide sufficient evidence to support a cyclin function for the polypeptide of SEQ ID NO:2. While the law does not require a specific example of everything within the scope of broad claims and does not require any specific working examples, sufficient evidence of function is required where the art teaches unpredictability.

With respect to the Examiner's assertion that the specification does not describe any use of a DNA sequence or a vector, Applicant points to pages 13, 16 and 21 of the specification (reply page 11).

The Office notes that while pages 13, 16 and 21 of the specification generally suggest uses for the claimed DNA sequences and vectors, the specification at these pages does not provide any actual guidance with respect to which of the claimed sequences to use and in what manner they should be expressed.

With respect to the Examiner's assertion that it would require undue experimentation to determine which sequence would encode a protein having mitogenic function, Applicant argues

that at the time of Applicant's invention one skilled in the art could easily have determined whether a sequence homologous to SEQ ID NO:2 exhibits mitogenic function without undue experimentation, as one only has to refer to Example 4 of the application to find a method for determining the presence of mitogenic cyclin function (reply pages 11-12). Applicant also points to the submitted reference of Soni et al. (Exhibit A) which shows that as of Applicant's filing date skilled artisans were aware of methods of determining mitogenic cyclin function (reply page 12).

The Office continue to maintain that it would require undue experimentation to determine which sequence would encode a protein having mitogenic function. The fact that as of Applicant's filing date skilled artisans were aware of methods of determining mitogenic cyclin function does not controvert that undue experimentation would be required, as the undue experimentation lies in the selecting of sequences from among the myriad claimed those sequences that would likely exhibit mitogenic cyclin function when subjected to testing. The specification does not provide sufficient guidance for one skilled in the art to distinguish operable from inoperable embodiments before subjecting the sequences to methods for determining cyclin function.

With respect to the cited reference of Doerks et al., Applicant points out that a DNA sequence encoding a mitogenic cyclin is defined in the specification not only by sequence information but also by function, such that the findings on Doerks et al with respect to protein function prediction based on sequence homology alone are not relevant to applicant's nucleotide sequences, as the claim preamble recites that the protein is a mitogenic cyclin. Applicant argues

that the specification in Example 4 demonstrates that SEQ ID no 2 has a mitogenic cyclin function, the specification in Example 2 demonstrates that the protein encoded by SEQ ID NO:1 associates with cdc2aAt and cdc2bAt, indicating that the cyclin of the instant invention binds to a cyclin dependent kinase specific consensus sequences present in SEQ ID NO:2, such as LXCXE motif common to all D-type cyclins involved in the binding of cyclins to retinoblastoma protein (reply pages 14-15).

The Office maintains that the assertion of a particular function for a protein is not sufficient to establish that the protein in fact has that function. The Office disagrees that amino acid sequence homology to *Arabidopsis* D-type cyclins coupled with the ability of SEQ ID NO:2 to interact with cdc2aAt and cdc2b in an *in vitro* yeast two-hybrid assay and the ability of SEQ ID NO:1 to hybridize with RNA transcripts that are induced by cytokinin and sucrose in vivo is sufficient to support the conclusion that SEQ ID NO:1 encodes a polypeptide that can activate a cyclin-dependent kinase. As discussed *supra*, while these observations suggest a correlation between the structure of SEQ ID NOS: 1 and 2 and D-type cyclins, they do not demonstrate that SEQ ID NO:1 encodes a protein that has a cyclin function.

Claims 1, 4 and 10 remain rejected, and newly added claims 38-41 are rejected, under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "mitogenic cyclin", for the reasons of record set forth in the office action mailed March 25, 2002.

Applicant's arguments filed August 29, 2002, have been fully considered but they are not persuasive.

Applicant argues that the claims do recite a structurally and functionally distinct type of cyclin in that the cyclin is described in terms of its sequence and the function is defined by it being a cyclin. Applicant argues that one skilled in the art would recognize that the term mitogenic in this context does not mean that the cyclin participates in mitosis, but rather that the cyclin is influenced by mitogenic compounds.

The Office maintains that the recitation of a specific sequence and the term cyclin does not serve to clarify the use of the phrase "mitogenic cyclin" in the claims. The Office maintains that both "mitogenic" and "cyclin" have various connotations in the art, such that "mitogenic cyclin" could be variously interpreted. Given the various distinct classes of cyclin proteins, all of which are implicated in the regulation of the cell cycle, and given that mitogenic could conceivably be applied to a cyclin protein as well as to agents that induce its expression, the use of the phrase "mitogenic cyclin" in the claims is indefinite.

Claim 27 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of the indefinite article "a" before "DNA sequence", for the reasons of record set forth in the office action mailed March 25, 2002. This rejection is not addressed in Applicant's reply. It is suggested that claim 6 be amended to recite "the DNA sequence".

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "hybridizing under stringent conditions". It is unclear what conditions would yield the claimed nucleic acid molecules, as those skilled the art define stringency differently. It is suggested that the claims be amended to recite specific hybridization conditions.

Claims 32-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of the indefinite article "a" before "vector" or "DNA sequence". It is suggested that the claims be amended to recite the definite article "the" rather than the indefinite article "a".

Claims 38-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "modulating". It is unclear in what way the plant cell cycle, plant cell division or growth, or level of activity of a mitogenic cyclin is modulated, as "modulating" encompasses many different types of changes, such as increasing, decreasing, prolonging, etc.

Claim Rejections - 35 USC § 101 and § 112

The rejection of claims 1-4 and 8-9 under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter is withdrawn in light of the claim amendments.

Claims 1, 6-8, 10 and 27 remain rejected, and newly added claims 30-41 are rejected, under 35 U.S.C. 101 because the claimed invention is not supported by either a specific asserted utility or a well established utility, for the reasons of record set forth in the office action mailed March 25, 2002.

Claims 1, 6-8, 10 and 27 also remain rejected, and newly added claims 30-41 are rejected, under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention, for the reasons of record set forth in the office action mailed March 25, 2002.

Applicant's arguments filed August 29, 2002, have been fully considered but they are not persuasive.

Applicant points out that the claims recite a specific function for the claimed DNA. Applicant also points out that, as discussed previously, a mitogenic cyclin actively regulates cell division and is influenced by compounds, and that a DNA sequence encoding an amino acid sequence having at least 70% sequence identity with SEQ ID NO:2 is not encompassed by the claims if it lacks mitogenic cyclin activity. Applicant argues that the Examiner is incorrect in asserting that no empirical data is provided to support a D-type cyclin function, as Example 2 of the specification teaches that the claimed DNA sequences encode a cyclin that binds both cdc2aAt and cdc2bAt cyclin dependent kinases. Applicant also points to page 2 of the specification which teaches that the binding of specific cyclin dependent kinases with specific cyclins is one way in which the activity of cdk/cyclin complexes is regulated. Applicant also points out that the prior art teaches that the function of D-type cyclins is induced by mitogenic cyclins. Applicant argues that the assignment of a cyclin function to the instant invention was not made on the basis of sequence comparisons alone (reply page 18).

The Office maintains that recitation of a specific function for the claimed DNA does not impart utility on the DNA in the absence of evidence sufficient to establish that the claimed DNA encodes a functional protein. Similarly, asserting that a mitogenic cyclin actively regulates cell division and is influenced by compounds, and that a DNA sequence encoding an amino acid sequence having at least 70% sequence identity with SEQ ID NO:2 is not encompassed by the claims if it lacks mitogenic cyclin activity does not impart utility on the DNA in the absence of evidence sufficient to establish that the claimed DNA encodes a functional protein. The Office

acknowledges Applicants assertion that the assignment of a cyclin function to the instant invention was not made on the basis of sequence comparisons alone, but maintains that the ability of a polypeptide of SEQ ID NO:2 to bind both cdc2aAt and cdc2bAt cyclin dependent kinases in an *in vitro* yeast two-hybrid system is not sufficient evidence to establish that a polypeptide of SEQ ID NO:2 functions to activate cdc2aAt or cdc2bAt cyclin dependent kinases.

Applicant also argues that how the DNA sequences and their encoded proteins would be substantially beneficial to the public is taught throughout the specification, for example page 21 teaches the utility of modulating the cell division and growth of cells such as plant in vitro cultures, the utility of overexpressing a cyclin gene to promote cell proliferation, and the utility of reducing cyclin expression to arrest cell division or prevent reentry into the cell cycle. Applicant argues that since cyclins have a known function, the claimed DNAs which encode a cyclin have a well established utility (reply pages 18-19).

The Office acknowledges the utilities asserted in the specification, but maintains that the claimed invention lacks utility in the absence of evidence sufficient to establish that the claimed isolated nucleic acids encode a protein having a cyclin function, i.e. able to activate a cyclin-dependent kinase.

Claim Rejections - 35 USC § 102

The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by GenEmbl Accession No. Y10162 (19 June 1997) is withdrawn in light of Applicant's foreign priority date of October 24, 1997.

Claim Rejections - 35 USC § 103

The rejection of claims 1-4, 6-10 and 27 under 35 U.S.C. 103(a) as being unpatentable over De Veylder et al. (4 August 1997, FEBS Letters Vol. 412 No. 3, pages 446-452, Applicant's IDS) in view of Fuerst et al. (November 1996, Plant Physiology, Vol. 112, No. 3, pages 1023-1033) is withdrawn in light of Applicant's foreign priority date of October 24, 1997.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (703) 605-1210. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

CC
November 12, 2002

PHUONG T. BUI
PRIMARY EXAMINER 11/18/02